

Remarks

This is in response to the official action mailed March 23, 2007 (Paper No./Mail Date 20070301).

Based upon Applicants' response filed February 15, 2007 the Examiner has withdrawn the finality of the previous office action (dated December 15, 2006) and has withdrawn all rejections that are not restated in the March 23, 2007 office action.

The Examiner has now issued five office actions in the case. Two office interviews have been conducted in person. Certain grounds of the rejection applied in the September 19, 2005 office action were withdrawn in the November 21, 2005 office action. The finality of the November 21, 2005 office action was withdrawn in the March 15, 2006 office action. Certain grounds of the rejection applied in the March 15, 2006 office action were withdrawn in the December 15, 2006 office action. The finality of the December 15, 2006 office action, along with several grounds of rejection, was withdrawn in the March 23, 2007 office action.

The pending claims are rejected under § 112 as failing to meet the written description requirements, under § 102 on the basis of Martin No. 20030082633, or as obvious under § 103 based upon various combinations of Yu, Williams '434, Martin '633; Cargill '555, Stadler, and Santagada.

THE § 112 ISSUES SHOULD HAVE BEEN RAISED IN THE FIRST OFFICE ACTION

The § 112 rejection is inappropriate for several reasons, including being raised in a fifth office action instead of a first office action. In accordance with the rules of practice, e.g., 37 CFR 1.104, the Examiner has the responsibility and obligation to, "be complete as to all matters," in the first office action, with only matters of form being excepted. Thus, no reason exists why terminology that has appeared in the specification and claims since the filing date should raise §112 issues at this late point in the prosecution of this application. Stated differently, the Examiner is taking the position that well understood terms that have been in the case for four (4) years have—in the fourth year and at the fifth office action—suddenly become ambiguous.

Nevertheless, Applicants welcome the opportunity to address the § 112 issues directly.

THE REFERENCES CITED BY THE EXAMINER DEMONSTRATE THAT THE SPECIFICATION MEETS THE WRITTEN DESCRIPTION REQUIREMENT

The Examiner's § 112 arguments are set forth on pages 2-6 of the March 23rd office action. The rejections are based on the first paragraph; i.e. the failure to comply with the written description requirement. Beginning on page 4, the Examiner takes the position that the phrase "microwave transparent" fails the written description test. On page 5, the Examiner takes the position that term "vessel" fails to meet the written description test.

The Examiner has cited several cases in support of the § 112 rejection. Although Applicants welcome the opportunity to address the law and the facts in an appropriate forum, Applicants will reserve a formal debate of the case law for any necessary appeal. The case law does establish, however, at least the following principle in addition to any argued by the Examiner:

If a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate written description requirement is met. *In re Alton*, 76 F.3d 1168, 1175 (Fed. Cir. 1996).

Applicant submits that the pending specification places the person of ordinary skill in the art in possession of the invention as of the filing date. Indeed, commercial versions of the invention have been available during the pendency of this application. As has been cited in previous office actions (i.e., as an exhibit to the response filed October 24, 2005), these commercial versions have been recognized by the industry—those persons skilled in the art—as a significant advance.

Although the Examiner offers a web-based dictionary (Answers.com) in support of the argument that the word "vessel" could mean too many items to enable the invention, the

first definition for the word "vessel" listed in the Examiner's own citation is, "a hollow utensil, such as a cup, vase, or picture, used as a container, especially for liquids."

Applicants thus submit that the Examiner's own investigation of the word "vessel" supports the enablement of Claim 1 rather than the Examiner's § 112 position.

Additionally, the references cited in the substantive rejections throughout the course of this prosecution all either refer directly to microwave transparent vessels or describe materials (such as Pyrex glass) that are widely recognized to be transparent to microwave radiation. For the sake of brevity, their full citations have been omitted here. In each case emphasis has been added.

Stadler: page 920:

These experiments were carried out at atmospheric pressure in standard Pyrex glassware with a reflux condenser fitted through the roof of the microwave cavity. The temperature of the stirred reaction mixture was monitored directly by a microwave-transparent fluoroptic probe inserted into the solution." (Emphasis added).

Al-Obeidi (at page 450):

The most commonly used solid support is made from polystyrene, which is a microwave-transparent material.

And later,

The reactions were carried out in open vessels in a conventional, kitchen microwave oven for 2.6 minutes and temperature near 55°C.

Martin 20030082633:

Microwaves can heat composite materials. For example, materials that are normally transparent to microwaves can be heated by adding polar liquids or conducting particles. (Paragraph 0135)

And,

Microwaves (including radiofrequency or RF electromagnetic radiation) are commonly used in wireless communication devices. Advances in microwave transmission have improved along with tremendous recent technological improvements in the satellite and communications industry (for example, in cell phones and wireless internet). (Paragraph 0005)

Microwaves are also well known in common kitchen appliances. Microwave ovens heat water-containing food rapidly because water is efficient at converting microwave energy to thermal energy. Kitchen microwave ovens emit microwaves at a frequency of 2.45 GHz, which is well within the microwave absorption spectrum of water. Frequencies outside of the absorption spectrum of water would not heat food as well. (Paragraph 0006)

Yu (at page 4781):

We describe here a novel application of microwave technology to enhance coupling efficiency in solid-phase peptide synthesis. A significant improvement of the coupling efficiency (a rate increase of at least 2-4-fold), especially in side-chain-hindered amino acids, was obtained in the study.

Figure 1 shows the reaction apparatus and vessels.

Williams, No. 6,858,434 uses the word "microwave" 33 times without any explanation as to wavelength or frequency. This demonstrates that the person skilled in the art understands the meaning of the term "microwave" without specific recitation of wavelengths or frequencies.

Daga (page 5191):

The reactions were carried out in an unmodified domestic microwave oven following the so called MORE (microwave organic reaction enhancement) techniques. The reactions were carried out in an Erlenmeyer flask covered with a filter funnel to prevent spillage during the experiments.

Erdelyi (page 1594)

All reactions were conducted in heavy-walled glass Smith Process Vials sealed with aluminum crimp caps fitted with a silicon septum. The inner diameter of the vial filled to the height of 3.5 cm was 1.3 cm. The microwave heating was performed in a Smith Synthesizer™ single mode microwave cavity producing continuous irradiation at 2450 MHz (Personal Chemistry AB, Uppsala, Sweden).

As the Examiner is aware, in order to serve as prior art, references must meet their own enablement standard. Therefore, if the Examiner is willing to rely on these references to support the § 102 and § 103 arguments, then the Examiner should be willing to take a consistent position with respect to these references when the Examiner carries out a § 112 analysis. Taken in this light, these references demonstrate that the skilled person understands quite well the meaning of terms such as "microwave," "microwave transparent," and "vessel." In addition to the understanding that the skilled person brings, the pending specification uses these well-understood terms to describe the invention in a manner that is above and beyond the minimum requirements of § 112.

#### THE § 102 REJECTION NO LONGER APPLIES TO THE AMENDED CLAIMS

The previously applied § 102 (b) rejection based on Martin '633 has been removed. In its place, the Examiner has applied an anticipation rejection under § 102(a) and (c).

The rejections are inappropriate for at least 2 reasons: (1) Martin '633 fails to disclose the claimed invention within its four corners; and (2) the relevant portions of Martin '633 lack enablement and thus cannot support any art-based rejection against the pending claims.

Claim 1 has been amended to recite the step of transferring solid phase resin between a resin source external to a single microwave transparent vessel and the microwave transparent vessel. This now appears as the initial step "(a)" in Claim 1, with the remaining steps being re-phrased appropriately in sequence.

This step, which is taken from Paragraphs 0038 and 0046 of the specification as filed, further differentiates the claimed invention from Martin. In the office actions dated

December 15, 2006 and March 23, 2007 (e.g., page 8), the Examiner has taken the position that when a peptide is bound to Martin's glass and susceptor sandwich, the glass and susceptor sandwich can be deemed to be a "vessel."

Martin describes (e.g. Paragraph 0295) a sandwich formed of an aqueous paste of barium titanate between two standard glass microscope slides. A cellulose membrane is glued to one of the slides. The peptide precursors are added as spots onto the cellulose membrane. According to the Examiner, Claim 1's recitation of a microwave transparent vessel reads upon Martin's combination of paper, glass, ceramic, and glue.

The Examiner also takes the position that Martin's sandwich is concurrently microwave transparent and microwave absorbing ("The vessel therefore reads upon a microwave transparent vessel and upon a microwave susceptor vessel."). Microwave transparency and absorbercy are opposite functions and only one of them—transparency—is recited in Claim 1

Applicants have previously argued that any analogy between a vessel and Martin's sandwich is tenuous at best. Nevertheless, in order to clarify Claim 1, the step of transferring solid phase resin from an external source into the vessel has been added.

As noted in previous responses and elsewhere herein, if Martin's sandwich is the "vessel," then it cannot serve as the "resin" and vice versa. Furthermore, Martin's glass/ceramic/glass/cellulose sandwich cannot be added to itself in the manner than actual resin can be added to an actual vessel as now recited in Claim 1.

#### MARTIN FAILS TO ENABLE THE STEPS ASSERTED IN THE OFFICE ACTION

In order for a reference to anticipate, the reference must enable the subject matter for which it is being asserted. In turn, enablement requires that the reference teach one of ordinary skill in the art to make or carry out the claimed invention without undue experimentation. The disclosure in the anticipating reference must be adequate to enable possession of the desired subject matter. Naming or describing subject matter is insufficient if the subject matter cannot be produced without undue experimentation.

In making the anticipation argument, the office action cites (on page 7) a portion of Martin's Examples 12 and 13 and Paragraphs 0294-0300. This argument requires both cross reference to, and incorporation of, the Hilpert publication and the Sigma-Genosys notes.

In the response filed February 15, 2007, Applicants have pointed out the ambiguities raised by (1) Martin's lack of explicit explanation and (2) Martin's brief referral to Hilpert and Sigma-Genosys. The Examiner dismisses these problems (on pages 8-9) with the unsupported conclusion that, "one of ordinary skill in the art would understand how to use the claimed invention based on the skill in the art . . . and upon the disclosure of Martin . . . including citations therein."

Therefore, because Martin fails to include, either explicitly or inherently, the elements recited in Claim 1, Martin cannot serve as a § 102 reference against Claim 1.

#### THE § 103 COMBINATIONS FAIL TO ADDRESS MARTIN'S WEAKNESSES

First, Applicants repeat and reincorporate in their entirety the arguments filed on February 15, 2007. In brief, they include the following:

1. The Sigma-Genosys technical notes fail to appear in the Information Disclosure Statements filed by Martin or in the Notices of References Cited provided by the Office (in the Martin '633 prosecution history). The Examiner has neither provided them to the Applicants nor included them as a cited reference in any office action. The failure to provide the Applicants with a copy of the Sigma Genosys technical notes is inconsistent with the requirements of MPEP 707.05(a) and (d). Accordingly, neither the Applicants nor the skilled person can confirm the identity or contents of the Sigma-Genosys technical notes. Therefore, they cannot provide the foundation for using Martin '633 in any type of art-based rejection.

2. The Hilpert reference fails to explicitly disclose the peptide preparation process.

3. Because of the multiple ambiguities in the manner in which Martin incorporates Hilpert and Sigma-Genosys and the manner in which Hilpert incorporates the two Kramer references, Martin '633 offers the skilled person at least six (6) permutations for carrying out Examples 12 and 13.

4. The large number of permutations that arise from the Examiner's use of Martin '633, Hilpert, Sigma-Genosys, Kramer, and Kramer-Schneider, the Martin '633 publication cannot enable the claimed invention and thus must fail as prior art for such purpose.

5. Martin absorbs microwaves while Claim 1 recites a vessel that transmits microwaves.

6. The Kramer-Schneider reference is inconsistent with the HMP resin techniques of Yu and fails to disclose or suggest the use of a microwave transparent vessel or of microwaves to accelerate any of the relevant steps.

7. Three of the cited techniques (Yu, Williams, Martin) differ fundamentally from one another and cannot be logically combined other than as an attempt reconstruct Claim 1 in hindsight.

8. The Examiner's position requires Martin's cellulose membrane to serve as both the linked solid phase resin (Claim 1, paragraph (a))—which it is not—and as the microwave transparent single vessel (Claim 1, paragraph (c))—which it is likewise not. The Examiner is taking a single element from the prior art and applying it to multiple different elements in Claim 1 on an ad hoc, as needed basis. The Examiner is stating—without support—that a cellulose membrane can be a linked solid resin peptide if necessary, or a single vessel if necessary, or both at the same time if necessary.

9. Claim 1 recites that the solid phase resin is linked to a first amino acid. If (as the Examiner asserts) the linked resin is the same as the single vessel, then the linked peptide would need to be in the vessel and be the vessel at the same time. This is logically inconsistent.

In addition to repeating previous § 103 rejections, the Examiner has applied several new § 103 rejections based on Yu, and that include Williams, Santagada, Stadler, and Cargill as secondary references

Applicants specifically repeat the points made in prior responses about combinations of Yu with Williams. Namely, Yu carries out peptide synthesis on a solid phase polystyrene resin, but fails to disclose or suggest deprotection using microwaves. Williams avoids using



a solid phase resin (thereby differing from both Claim 1 and Yu) and instead uses thin layer chromatography plates coated with silica gel. Accordingly, no reason exists to carry out the Williams technique on Yu's polystyrene resin or the Yu technique on Williams's silica gel. The combination thus stands as a mere hindsight reconstruction based upon Claim 1.

Accordingly, the "new rejections" based on combinations of Yu and Williams must fail as lacking any logical support other than the pending claims.

#### Rejections that include Santagada

The Santagada reference has been applied for the use of specific activators in a single microwave enhanced coupling reaction. Accordingly, regardless of the combination in which it is used, Santagada offers no cure for the weaknesses in the base references or the combinations.

#### Rejections that include Stadler

As admitted by the Examiner (page 12 of the office action) Stadler offers nothing beyond attaching or cleaving carboxylic acids to and from resins. Accordingly, it cannot support or cure or the failures of Martin or the other base references or produce a useful combination with them.

#### Rejections that include Cargill

The Examiner has cited Cargill No. 6,171,555 for the first time in this office action. In its own words, Cargill illustrates, "a docking station (that) includes remotely actuated locking mechanisms for secure registration of reaction blocks, and provides for introduction of gases, liquids, and vacuum to the reaction blocks" (e.g., Abstract). According to the Examiner, Cargill teaches solid phase synthesis of peptides in a single microwave-transparent vessel using microwaves. The cited portions, however, offer little or no support to the Examiner's arguments. First, at cited column 1 lines 38-67, Cargill does nothing more than

point out the same prior art that the pending specification pointed out when filed; i.e., peptides have historically been synthesized on solid phase resins.

The Examiner also cites "column 2," but there appears to be nothing there that specifically applies to the claimed invention or to the Examiner's arguments other than a continuation of the background discussion of column 1.

The Examiner cites column 3 lines 1-30, but again this is a general discussion that neither applies to the pending claims nor supports any arguments based on the other references.

The Examiner cites column 4 lines 37-39, 25-39 and 43-67, but these offer nothing other than the broad statement that in the Cargill docking station, "product reaction could be enhanced by the application of microwaves." Cargill fails to offer this in connection to any specific chemical reaction, but only as a general statement. Applicant accordingly submits that Cargill cannot cure the weaknesses of the combinations set forth in this office action.

The remainder the claims are dependent from Claim 1, and thus all of the same arguments apply. Because the combinations fail to render Claim 1 obvious, they likewise fail to render any of the dependent claims obvious.

Therefore, Applicants submit that the § 103 rejections against the pending claims must likewise be removed.

Applicants accordingly submit that the claims are in condition for immediate allowance, and the same is respectfully requested.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Philip Summa", with a long horizontal flourish extending to the right.

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